AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions and listings of claims in the application:

1-26. (Cancelled)

27. (Currently amended) A computer-assisted method for performing restrained dynamics docking of a substrate on an enzyme, a 3-D structure of which is available, comprising the steps of

j. determining a force field, and independently simulating the presence of said enzyme in said force field,

k. minimizing the potential energy (Ep) linked to said force field of said 3-D structure, wherein the spatial position of some atoms of said enzyme is fixed, and wherein the other atoms are mobile, by allowing mobility of the mobile atoms, by

i. simulating an increase in temperature (in order to give kinetic energy),

ii. and minimizing the potential energy by re-specifying the temperature as 0 Kelvin (K),

l. optionally repeating step k in order to obtain other Ep minima, wherein said Ep minima are such that the structure of the protein remains folded,

m. minimizing Ep in said force field of said 3-D structure, wherein all the atoms of the protein are mobile, by

i. simulating an increase in temperature (in order to give kinetic energy), and

ii. minimizing the potential energy by re-specifying the temperature as 0 Kelvin (K),

n. simulating, at 0 K the presence of said substrate next to said enzyme,

o. optionally generating a molecular dynamics simulation on said substrate and enzyme (simulating an increase in temperature, in order to allow mobility of the atoms),

p. generating some constraints to said substrate, in order to impose that said substrate[[it]] has interaction with said enzyme, wherein said constraints are final distance constraints between some atoms of said substrate and some atoms of amino-acids present in said active site,

q. generating a molecular dynamics simulation on said substrate and enzyme, with said constraints imposed in step p[[.]],

r. optionally, generating a molecular dynamics simulation on said substrate and enzyme without said constraints of step p[[.]]; and

s. generating a result in a user readable format.

28. (Original) The method of claim 27, wherein said fixed atoms in step k. are the backbone atoms N-Cα-CO in the first minimization step and only Coc in subsequent minimization steps.

29. (Original) The method of claim 27, wherein said kinetic energy is simulated by temperature increase to about 100 K for about 5-20 ns.

30. (Original) The method of claim 27, wherein said force field in step j. comprises forces linked to a. the distance between atoms, b. the angles of valence, c.

the dihedral angles, d. the deformation with regard to planar geometry, e. the electrostatic field, f. the Van der Waals forces, g. hydrogen bonds.

31-32. (Cancelled)

33. (Original) The method of claim 27, wherein step o. is performed with a simulated temperature of between about 15 and 50 K.

34. (Original) The method of claim 27, wherein step q. is performed with a simulated temperature of between about 15 and 50 K.

35. (Original) The method of claim 27, wherein step r. is performed with a simulated temperature of between about 200 and 350 K.

36. (Original) The method of claim 27, wherein said enzyme is a cytochrome P450 subfamily 3A comprising mammal and human cytochromes.

37. (Currently amended) The method of claim 36, wherein said cytochrome is a cytochrome P450 3A4~~, and said structure is the structure obtained by the method of claim 15, in particular the model structure of claim 22~~.

38. (Original) The method of claim 36, wherein said substrate is a small organic compound which size can range for example from MW 288 (testosterone) to MW 1203 (cyclosporine A).

39. (Original) The method of claim 38, wherein said substrate is testosterone.

40-67. (Cancelled)